Gene Transfer and Rare Diseases Workshop

National Institutes of Health

DRAFT AGENDA
September 13, 2012
Rockville Hilton, Rockville, MD

8:00 AM **Welcome and Introductions**

Session I: Clinical Experience

Gene transfer for rare diseases – what are the challenges and keys to success?

8:10 AM **Hemophilia**
Katherine A. High, M.D.
Professor of Pediatrics
The Children's Hospital of Philadelphia

8:30 AM **Leber Congenital Amaurosis and Other Eye Disorders**
Samuel G. Jacobson, M.D., Ph.D.
Professor of Ophthalmology
Scheie Eye Institute
University of Pennsylvania

8:50 AM **Blood Cell Disorders**
Donald B. Kohn, M.D.
Professor in the Departments of Microbiology, Immunology & Molecular Genetics
University of California

9:10 AM **Lipoprotein Lipase Deficiency: EU Development and Regulatory Experience**
Carlos R. Camozzi, M.D., Ph.D.
Vice President and Chief Medical Officer
uniQure B.V.

9:35 AM **Panel Discussion**

Moderator: Donald Kohn, M.D.

Questions

1. What are some of the key scientific challenges in developing clinical protocols for a rare disease?

2. How frequently were disease-specific animal models available for rare diseases and if there was no appropriate animal model was this a rate limiting step?

3. If you've had success with a vector or transgene, in a clinical trial, how do you most efficiently transfer those successful elements into other studies for diseases with similar phenotype?

10:00 AM **Break**

Session III: Resources

10:15 AM ***What NIH resources are available, and how are they being used?***

Gene Therapy Resource Program (GTRP)
Sonia I. Skarlatos, Ph.D., F.A.H.A.
Acting Director, Division of Cardiovascular Diseases
National Heart, Lung and Blood Institute

Bridging Interventional Development Gaps (BrIDGs)
John McKew, Ph.D.
Chief of the Therapeutic Development Branch
NCATS

Genetic Modification Clinical Research Information System (GeMCRIS)
Robert Jambou, Ph.D.
Office of Science Policy
National Institutes of Health

Rare Disease Clinical Research Network (RDCRN)
Rashmi Gopal-Srivastava, Ph.D.
Director, Extramural Research Program
Office of Rare Disease Research
National Center for Advancing Translational Sciences (NCATS)

National Gene Vector Biorepository (NGVB)
Kenneth Cornetta, M.D.
Joe C. Christian Professor & Chairman of Medical & Molecular Genetics
Indiana University

Session III: Defining Opportunities for Data Sharing Across Protocols

11:30 AM **Preclinical Studies to Support Clinical Applications of Gene Therapy Products**

Mercedes Serabian, M.S., D.A.B.T.
Supervisory Toxicologist, Center for Biologics Evaluation and Research
Federal Food and Drug Administration

11:50 AM **Lunch**

12:45 PM **Panel Discussions**

Panel I

Moderator: Yuman Fong, M.D., Chair, NIH Recombinant DNA Advisory Committee

Lead Panelists

Ronald G. Crystal, M.D.
Professor of Medicine
Weill Cornell Medical College

Barry Byrne, M.D., Ph.D.
Director, Powell Gene Therapy Center
Professor, Pediatrics and Molecular Genetics & Microbiology
Associate Chair, Pediatrics
University of Florida

Daniel Takefman, Ph.D.
Chief, Gene Therapy Branch
Division of Cellular and Gene Therapies
Cellular, Tissue, and Gene Therapies
Center for Biologics Evaluation and Research
Food and Drug Administration

Janet Benson, Ph.D.
Director, Applied Toxicology and Gene Therapy Pharm/Tox Program
Lovelace Respiratory Research Institute

Questions

1. Are there common studies or assays, which could produce data that can be shared across different trials involving similar diseases or vectors?
    a. What types of preclinical data could be useful for sharing?
    b. What are the FDA and regulatory agencies considerations regarding sharing data (e.g., cross-reference letters, platforms)?
    c. What are possible mechanisms for sharing?What is the tolerance and limitations for sharing in drug development, for academic researchers, biotech/pharma?

2. What factors must the studies have in common for shared data to be useful?
    a. For example, would data from biodistribution studies using the same vector backbone still be applicable if the promoter or transgene were changed in the subsequent study but the route of administration was similar?

b. For studies involving integrating vectors, what factors would need to be considered in determining whether genotoxicity data could be shared?
c. How useful have the current Ad-5 and AAV-2 reference standards been to the field? Would the development of additional standard reagents be helpful for the field in terms of regulatory review and sharing of data across preclinical studies?

3. How is the NGVB toxicology database currently being used? What improvements might encourage increased use of pharm/tox databases that are detailed, readable, and searchable?

4. How could NIH foster data sharing?

2:00 PM **Panel Discussion**

Panel II

Lead Panelists

Brian P. Sorrentino, M.D.
Director, Experimental Hematology Division
Director, Vector Production Facility
St. Jude Children's Research Hospital

Jeffrey Bartlett, Ph.D.
Vice President, Research and Development
Calimmune, Inc.

R. Jude Samulski, Ph.D.
Director, Gene Therapy Center
Professor of Pharmacology
University of North Carolina

Questions

Is there a role for developing therapeutic platforms to be used for multiple diseases to maximize the sharing of data and efficiencies in developing new gene transfer studies for rare diseases?

1. What common characteristics of diseases allow one to develop platforms?

2. What would be the considerations for designing a platform for multiple trials involving similar vectors, diseases, and transgenes (e.g., lentivectors for different immunodeficiencies)?

3. Are some of the AAV and lentiviral vectors being used across the field sufficiently similar to be included in a platform?

4. When is the time to consider vector platforms versus continued refinement?

3:00 PM **PUBLIC COMMENT**

3:15 PM **BREAK**

Session IV: Mechanisms for Advancing Gene Transfer for Rare Diseases

3:30 PM **Panel Discussion**

Moderator: Yuman Fong, M.D., Chair RAC

Questions

1. How are current resources being used and are the ways that they might be improved to make them more useful to investigators developing protocols for rare diseases?
    a. RDCRN
    b. BrIDGs
    c. GeMCRIS
    d. NGVB
    e. GTRP
2. Are there particular gaps in available programs that hinder development of protocols for rare diseases?
3. What are the challenges to obtaining funding for preclinical studies to support IND applications in gene transfer for rare diseases?
4. Are there regulatory policies that can facilitate data sharing?
5. What are the operational needs in data sharing?
6. How can publication of safety data and negative results be encouraged for both authors and journals?
7. What are our conclusions from this meeting?

5:00 PM **PUBLIC COMMENT**

5:15 PM **ADJOURN**